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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,003	03/22/2001	David M. Sabatini	50347/002004	5682

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EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	09/817,003	SABATINI, DAVID M.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *160-177 and 237-272* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-177 and 237-272* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-159 and 178-236 have been cancelled. Claims 160 and 271 have been amended.

Claims 160-177 and 237-272 are pending and under examination.

2. The applicant notes that although claim 272 is listed as rejected on the PTO-326, the claim is not included in any of the rejection of record. In response, although claim 272 was inadvertently omitted from the heading, the claim was addressed in the body of the rejection under 35 USC § 103 over Palsson, in view of both Taylor et al. (U.S. Patent No. 6,103,479) and Fire (U.S. Patent No. 6,506,559) (see p. 6 of the non-final Office action mailed on 12/30/2009). Thus, the claim was correctly indicated as rejected on the PTO-326.

Response to Arguments

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 160-163, 166, 169, 172, 173, 175, 241, 242, 244-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269 and 271 remain rejected under 35 U.S.C. 102(b) as being anticipated by Palsson (WO 96/17948).

Palsson teaches a reverse transfection surface which is an array comprising a support suitable for culturing cells which does not contain wells, the support comprising nucleic acids deposited at a plurality of distinct locations (i.e., discrete) and plating dispersed eukaryotic cells on top of the nucleic acids (i.e., the plurality of locations comprise eukaryotic cells and nucleic acids in discrete locations). The cells become transfected with the nucleic acids after culturing the array for a suitable period of time (claims 160, 172, 246, 247, 253, 259 , 265 and 271) (Abstract, p. 5, line 29 through p. 6, line 10; p. 8, lines 1-15, p. 10, lines 1-5; p. 11, lines 22-25; p. 12, lines 26-32; p. 14, line 25 through p, 15, line4; p. 17, lines 26-28; Example III, Fig. 4-6). The nucleic acids could be plasmids (claims 161-163, 166, 173, 248, 254, 260 and 266) or RNAs (claim 169), the nucleic acids further comprise carriers such as liposomes (i.e., lipids) (claims 175, 242, 251, 257, 263 and 269), the nucleic acids could be non-covalently bound to the support via antibodies, adhesion molecules or polycations such as polylysine (claims 173, 241, 244 and 245) (p. 8, lines 20-25; p. 9, lines 5-7; p. 12, lines 24-30). Since Palsson teaches all claim limitations, the claimed invention is anticipated by the above cited art.

The applicant argues that Palsson does not describe a surface having a plurality of locations, each comprising "a feature comprising one or more defined nucleic acids in

a discrete location." For example, p. 5, line 29 -p. 6, line 10, of WO 96/17948 state as follows: "This invention provides a method of transfecting target cells by particles comprising depositing the particles on a cell growth support and contacting the target cells with the particle-loaded cell growth support. In one embodiment of the method, the particles are retroviral particles. Another embodiment further comprises cryopreserving or lyophilizing the particle-loaded cell growth support prior to contacting target cells. The invention also provides a composition comprising particles capable of transfecting target cells localized on a filter, membrane filter, cell culture surface or tissue engineering material in an amount effective for increasing the transfection efficiency of target cells ....." Page 8, lines 1-15, of WO 96/17948 state as follows: "The invention provides a new method that dramatically increases the transfection efficiency by increasing the contact between particles and target cells. The contact is increased by localizing particles on a cell growth support and directing target cells to contact the particle-loaded cell growth support. As broadly claimed, the method comprises two steps. First, the particles are deposited on the cell growth support by various means such as filtration or absorption. Second, the target cells are directed to the particle-loaded cell growth support by various means such as gravity sedimentation or filtration. Localizing the particles on the cell growth support increases the contact between particles and target cells, which increases the transfection efficiency compared with that ....." The applicant argues that there is no teaching in the portions of Palsson reproduced above (or in the other portions cited by the examiner) describing nucleic acids present on the support in a plurality of discrete locations so as to result in features, each comprising an area of a

substrate having a defined nucleic acid sequence affixed thereto (or sequences in the case of certain co-transfection embodiments). The applicant submits that one of skill in the art would understand that the term "discrete location" as used in the instant claims indicates that the nucleic acids are confined to particular areas of the surface rather than being distributed throughout the surface. Thus, the surface must contain regions between the features, which regions do not contain the defined nucleic acids that are present in the features. Palsson does not teach confining defined nucleic acids to particular locations on the surface and thus does not teach a surface comprising a plurality of features as set forth in the instant claims. For at least this reason, Palsson does not teach all the features of the claims and thus cannot anticipate the claims.

The applicant's arguments are acknowledged; however, they are not found persuasive for the following reasons:

The argument that one of skill in the art would understand that Palsson's viral particles are distributed throughout the surface such that there are no particle-free regions has no basis. Palsson clearly teaches depositing viral particles suspended in solution and not a homogenous nucleic acid solution. By reading Palsson and looking at Palsson's Fig. 4 and 6, one of skill in the art would readily understand that depositing particles in suspension would result in a deposition pattern having particles deposited at discrete locations with particle-free regions between these discrete locations. Thus, Palsson does teach all the features of the claims and anticipates the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 160-166, 169, 172, 173, 175, 241-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269 and 271 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palsson.

The teachings of Palsson are applied as above for claims 160-164, 166, 169, 172, 173, 175, 241, 242, 244-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269 and 271. Although Palsson et al. teaches adhesion molecules, he does not specifically teach fibronectin (claim 243). However, fibronectin was well-known in the prior art as an adhesion molecule. Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to modify Palsson's transfection surface by using fibronectin as an adhesion molecule to achieve the predictable result of obtaining a device suitable for transfection. Palsson does not specifically teach that the nucleic acids encode a polypeptide (claim 164). However, using such to express polypeptides into cells was routine in the prior art. Therefore, it would have been obvious to one of skill in the art, at the time the invention was made to include nucleic acids encoding polypeptides into Palsson's transfection surface to achieve the predictable result of obtaining a device suitable for expressing polypeptides of interest into cells. Palsson

does not specifically teach the cell density recited in claim 165. However, absent evidence of unexpected results, it would have been obvious to one of skill in the art to vary the cell density with the purpose of optimizing the transfection results. Again, absent evidence to the contrary, it is generally not inventive to discover the optimal working conditions of a prior art method, such conditions can be identified by routine experimentation (see MPEP 2144.05 [R-5]).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

The arguments are the same as above and are not found persuasive for the reasons set forth above.

7. Claims 160-164, 166-177, 237-242 and 244-271 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palsson, in view of both Taylor et al. (U.S. Patent No. 6,103,479, of record) and Fire (U.S. Patent No. 6,506,559, of record).

The teachings of Palsson are applied as above for claims 160-164, 166, 169, 172, 173, 175, 241, 242, 244-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269 and 271.

Although Palsson teaches that the transfection surface can be made with any apparatus which allows nucleic acid deposition on the support (p. 20, lines 4 and 5), he does not teach a microarrayer, wherein the use the microarray results in an array arranged in rows and columns and comprising different nucleic acids at different

locations (claims 168, 174, 237-240, and 272). However, doing such is suggested by the prior art. For example, Taylor et al. teach high throughput screening (HTS) by using arrays comprising tens of thousands of discrete spots, wherein the arrays can be made by using a microarrayer and wherein the location of the spot in the array provides the address for later reference to each spot; they also teach HTS of the physiological responses of cells to biologically active compounds (Abstract; column 6, lines 40-53; column 9, lines 20-29). It would have been obvious to one of skill in the art, at the time the invention was made, to modify Palsson by using a microarrayer to obtain the predictable result of obtaining a transfection surface suitable for HTS of cellular response to diverse biologically active factors encoded by nucleic acids. With respect to the limitation recited in claim 167, it would have been obvious to one of skill in the art to spot at least two different nucleic acids at the same discrete location when transfection with more than one nucleic acid was needed.

Palsson and Taylor et al. do not teach siRNA (claims 170, 171, 176, 177, 249, 250, 252, 255, 256, 258, 161, 262, 264, 267, 268 and 270). However, doing such is suggested by the prior art. For example, Fire et al. teach screening siRNA in a HTS setting (column 12, lines 46-61). It would have been obvious to one of skill in the art, at the time the invention was made, to modify transfection surface of Palsson and Taylor et al. by using siRNA achieve the predictable result of obtaining a device suitable for screening siRNA in a HTS setting.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

The applicant argues that Taylor' s column 1 (lines 47-56), cited by the examiner, describes arrays composed of 10-14 nucleotide oligonucleotides attached to a glass plate, available commercially from Affymetrix under the trade name GENECHIP. The oligonucleotides are intended to hybridize to fluorescently labeled complementary nucleic acids, which can then be detected after washing to remove nucleic acids that did not hybridize to oligonucleotides on the array (Taylor, col. 1, lines 56-60). The applicant argues that, although the examiner asserts that the arrays are made by using a microarrayer, Taylor is silent as to how the oligonucleotide arrays were made. The examiner has not provided any evidence that the arrays were made by using a microarrayer. Accordingly, to the extent that the rejection is based on the premise that the oligonucleotide arrays described by Taylor were made using a microarrayer, this is unsupported and the rejection should be withdrawn.

The applicant argues that the examiner has failed to establish that one of skill in the art would be motivated to modify Palsson according to the teachings of Taylor to arrive at the instant invention with a reasonable expectation of success. First, Taylor does not suggest or provide motivation for combining oligonucleotide arrays with cell arrays for HTS screening. Taylor does not teach or suggest that oligonucleotide arrays could have any use other than for detecting fluorescently labeled complementary nucleic acids. Taylor does not teach or suggest that such arrays could have any use whatsoever in the context of cultured cells. Second, there is nothing in Taylor to suggest that the conditions under which oligonucleotide arrays are made result in a surface compatible with the growth and transfection of eukaryotic cells. The examiner

has failed to establish that such an oligonucleotide array could predictably be used to produce an array of transfected eukaryotic cells growing in culture on the surface of such oligonucleotide array. Third, in order for the GENECHIP array to be useful for the purpose described by Taylor, i.e., hybridization of oligonucleotides to fluorescently labeled complementary nucleic acids, one of skill in the art would find it desirable that the oligonucleotides remain attached to the glass plate during the processes of hybridization, washing to remove unhybridized nucleic acids, and detection. Thus, the principle of operation of an oligonucleotide array such as that mentioned by Taylor is based on oligonucleotides that remain attached to the surface. If oligonucleotides detach from the surface they would not contribute to the detection of labeled complementary nucleic acids and, if anything, would reduce their detection. However, the instant invention requires that nucleic acids are introduced into and transfect eukaryotic cells. Nucleic acids that remain attached to a surface would not be capable of entering and transfecting cells. MPEP 2143.01 VI, states that "The Proposed Modification Cannot Change the Principle of Operation of a Reference." As stated therein, "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)." The applicant acknowledges that as set forth in the rejection, the "prior art invention being modified" is Palsson rather than Taylor. However, the reasoning of MPEP 2143.01 VI is applicable - the modification proposed by the examiner would change the principle of operation of the oligonucleotide array of

Taylor from one that is based on oligonucleotides that remain attached to the surface to one in which at least some detachment from the surface is required. One of skill in the art would not be motivated to make the modification proposed by the examiner. Fourth, even if the skilled artisan was motivated to modify Palsson by using the oligonucleotide array of Taylor, there is no evidence in Taylor that oligonucleotides of the GENECHIP array would in fact detach from the surface and enter eukaryotic cells, let alone that they would do so in a manner that would predictably result in an array of transfected eukaryotic cells. The examiner has failed to establish that an oligonucleotide array such as that mentioned by Taylor could predictably be used to produce an array of transfected eukaryotic cells growing in culture on the surface.

The applicant argues that Fire does not cure the deficiencies noted above.

The applicant's arguments are acknowledged; however, the rejection is maintained for the following reasons:

All arguments regarding Taylor are not material to the instant rejection because the instant rejection is not based on modifying Taylor, i.e., using Taylor's GENECHIP oligonucleotide array in Palsson's method. The rejection clearly states that Taylor provides the suggestion to modify Palsson by spotting Palsson's viral particles on Palsson's substrate by using a microarrayer. Such a modification does not change Palsson's principle of operation.

The argument that Taylor does not teach a microarrayer is not found persuasive because Taylor does teach using a microarrayer (column 9, lines 20-29).

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633